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Mathematical Modeling for the Prediction and Optimization of Laser Hair Removal

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Background and Objective: **The study of hair removal is a slow, tedious process. Efficacy evaluations require test-site observation for at least one complete hair cycle, a minimum of 6–8 months. In addition, tracking and counting individual hairs is extremely labor intensive. The objective of this study was to develop and evaluate a mathematical model for hair removal that could significantly speed the entire process.**
Study Design/Materials and Methods: **Generally accepted kinetic and statistical modeling methods were used to develop a mathematical description of hair growth. The anagen and telogen percentages and decay times were the variables used to predict the kinetics of untreated hair. In the case that the follicles were treated, it was necessary to additionally consider the possible outcomes after treatment, making the calculations much too complicated for simple mathematical formulations. Therefore, a computerized statistical model was developed that considered the probabilities of no, partial, or complete follicular damage in addition to the untreated model variables. These models were then evaluated by comparing them to data derived from the literature and a study center.**
Results: **Values derived from the mathematical model were capable of closely approximating the experimental results of untreated (shaving) and treated (plucking, electrolysis, ruby laser, Q-switched Nd:YAG laser) hair growth kinetics. The model was also shown to be useful for optimizing the number and interval of Q-switched Nd:YAG laser treatments.**
Conclusions: **A mathematical model can be used to reliably predict results from a variety of hair removal techniques. It also appears to be useful for optimizing a particular treatment protocol. In addition, the development of new hair removal products may be aided by using this method. Lasers Surg. Med. 26:164–176, 2000**

Key words: laser hair removal; mathematical model; anagen; telogen; synchronization

INTRODUCTION

Hair removal represents a substantial portion of the cosmetic market. Traditional methods such as shaving, waxing, tweezing, chemical depilatories, and electrolysis/thermolysis have been complemented recently by hair removal with powerful coherent and incoherent light devices [1]. The latter techniques have the potential to revolutionize the entire hair removal business.

Each of these new techniques requires much study for optimization. Unfortunately, this is an extremely slow, inefficient, and expensive process. One reason is that a realistic efficacy evaluation of a certain method demands that test sites be followed for at least the length of one complete hair cycle. In all body areas, this represents a minimum of 6–8 months and often longer [2,3]. In addition, tracking and ultimately counting individual hairs can be quite tedious and, to get ac-

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curate results, must be done in a painstaking manner. A method to speed this process would be most welcome.

This study examines a mathematical model of hair growth based on currently accepted kinetic and statistical methods [4,5]. The model allows investigation of hair growth kinetics during and after different treatment types, ranging from shaving to laser hair removal. The model can be used for optimization of a treatment procedure and for the prediction of short- and long-term results of single, multiple, or combined treatments. Most parameters required for the model are either already available or can be measured experimentally in a relatively short time period. The model has been tested during clinical trials with the Q-switched Nd:YAG laser. It has been thoroughly compared with hair removal data reported in the literature as well.

BACKGROUND

Available intense light sources can precisely affect hair growth by means of selective photothermolysis [1]. Pigmented hair contains a high concentration of the natural chromophore melanin, which absorbs both visible and infrared radiation. In lighter skin types, epidermal melanin content is lower so that photoabsorption is less and the skin can be protected from intense light damage during laser hair removal. When skin is irradiated with a powerful light beam in the 700- to 1,100-nm spectral range, a sufficiently high fluence can be reached as deep as the follicular papilla without substantial thermal effect to the skin. Follicular melanin absorbs the light and the temperature of the hair rises to a level sufficient to thermally damage the pilar unit. The papilla, bulge, and root sheaths are three follicular structures that should be destroyed to achieve long-term hair reduction [1].

The study of hair growth requires appropriate methods and plenty of time and patience. This is a major reason why there are only a handful of published studies that deal with the temporal behavior of hair growth [2,3,6–9] (Table 1). These studies reveal that individual hairs grow in cycles that are sequentially repeated throughout the life span of the hair follicle. Each cycle includes an anagen phase of active hair growth and a telogen phase in which there is no growth. A short transition period between anagen and telogen is termed catagen. Anagen hairs grow at a rate of 1.5–2 mm per week. In telogen, hair does not grow, but remains attached to the follicle. The old hair is shed when it is effectively “pushed out” by a new growing hair.

The duration of anagen ranges from 8–16 weeks in most body areas except the scalp and face. Telogen has been observed to last approximately 2–4 weeks longer. The duration of the breakdown or catagen stage is only 2–3 weeks [2,3,5,6,8]. The timing of the hair cycle has been thoroughly studied, especially with regard to variations between body areas, ages, sex, seasons, and other factors. Significant variations in the duration of anagen and telogen have been observed between individuals. In the same individual, the variation in the duration of anagen, telogen, or the entire cycle as a function of body area seems to be approximately 10%[2,3]. In other words, anagen follicles in a given subject and particular body region have a duration that varies between the follicles and sequential cycles of the same follicle by about 10%. The same holds true for telogen follicles and the entire hair growth cycle. It has also been found that the relative proportion of telogen hairs gradually increases with age and that there are seasonal variations in the anagen/telogen ratio on the scalp [3,6,10,11]. Although no data have been reported in the literature yet, the trend is probably similar for other body areas as well. The initiation of individual hair cycles has been found to be a completely random phenomenon. This finding explains why humans do not molt as do animals. Asynchronous human hair cycles result in essentially continuous body hair shedding. For this same reason, a relatively constant percentage of anagen and telogen hairs is found in each body area.

Hair removal treatment can be graded according to the amount of follicular damage. No damage is done when shaving or when using a chemical depilatory. Alternatively, mild follicular damage can be sustained if hairs are plucked or waxed. Besides X-irradiation, electrolysis/thermolysis and intense light or lasers are the only available techniques that can cause significant damage to the pilar unit [1].

If no damage is done to the follicle, the effect is purely cosmetic and consists of removing the visible portion of the hair. The hair in anagen continues to grow at a constant rate so that, depending on the rate, treatments may be needed every 1–7 days. If both anagen and telogen hairs are present before treatment, an apparent hair loss of more than 50% will be observed. This is

TABLE 1. Properties of Hair Growth in Humans

Anatomic area [Ref]	Sex	Age (yr)	Race	Density hair/cm^2	% anagen	% telogen	Time in anagen	Time in telogen	Time in catagen	Hair cycle (avg)	Hair cycle (winter)	Hair cycle (summer)	Growth rate (mm/day)
Scalp													
[5]	M–F	22–27	?	223 (175–300)		13–16							0.32–0.37
[5]	M–F	41–48	?	223 (175–300)		22–25							0.32–0.37
[6]					60–80	12–15	2–6 years	3–4 months	2–3 weeks				
Under the temple													
[3]	M	60	Japanese				23.1 weeks (12–48)	7.0 weeks (6–8)		30.1 weeks (19–54)			
[3]	M	30	Japanese				19.6 weeks (14–34)	8.3 weeks (6–13)		27.9 weeks (22–40)			
[3]	M	21	Japanese				12.9 weeks (8–24)	8.0 weeks (5–12)		20.7 weeks (15–31)			
Beard													
[6]							12 months	3 months					
Eyebrow													
[3,6]							4–8 weeks	13–15 weeks					
[7]													0.16
Upper lip													
[3]	M	60	Japanese				19.2 weeks (11–29)	6.2 weeks (5–9)		25.4 weeks (17–37)	26.3	25.2	
[3]	M	30	Japanese				11.7 weeks (2–23)	6.0 weeks (3–14)		17.8 weeks (8–31)	20.7	21.6	
[3]	M	21	Japanese				8 weeks (4–14)	6.4 weeks (4–11)		14.3 weeks (9–22)	15.0	12.9	
[3]	M						16 weeks (2–29)	6 weeks (3–14)		22 weeks (8–37)			
Finger													
[3]	M	60	Japanese				11.7 weeks (9–15)	11.3 weeks (6–14)		23.0 weeks (20–28)	23 weeks	25 weeks	
[3]	M	30	Japanese				6.8 weeks (3–12)	8.4 weeks (5–13)		15.2 weeks (11–22)	14.9 weeks	14.9 weeks	
[3]	M	21	Japanese				7.1 weeks (4–13)	8.0 weeks (3–13)		15.2 weeks (10–19)	15.3 weeks	15.1 weeks	
Hand													
[6]							10 weeks	7 weeks					

TABLE 1. (Continued)

Anatomic area [Ref]	Sex	Age (yr)	Race	Density hair/cm^2	% anagen	% telogen	Time in anagen	Time in telogen	Time in catagen	Hair cycle (avg)	Hair cycle (winter)	Hair cycle (summer)	Growth rate (mm/day)
Arm													
[2]	M	20–30	White	15–18		69–75	28 days (55)	80 days (144)		108 days (199)			0.32
[2]	F	20–30	White	16–21		75–79	22 days (45)	84 days (152)		106 days (197)			0.28
[3]	M	60	Japanese				10.5 weeks (6–15)	14.9 weeks (10–19)		25.3 weeks (16–29)	24 weeks	26.5 weeks	
[3]	M	30	Japanese				11.1 weeks (7–14)	13.0 weeks (9–19)		24.0 weeks (17–29)	22.3 weeks	22.3 weeks	
[3]	M	21	Japanese				9.6 (6–12)	12.4 (8–24)		22.1 (15–34)	21.7 weeks	23.7 weeks	
Chest													
[3]								10 weeks			20–30	18–27	
Pubic													
[8]	F	17–45				54						0.3	
[3]							12–14 weeks	16–18 weeks					
Axilla													
[8]	F	17–45	White			54							0.3
[8]	F	17	Black			58							0.3
[6]							A few months	3 months					
Leg													
[3]	M	60	Japanese				16.4 weeks (14–18)	11.3 weeks (8–15)		28.2 weeks (24–33)			
[3]	M	30	Japanese				16.7 weeks (13–24)	23.1 weeks (21–30)		39.9 weeks (32–49)			
[3]	M	21	Japanese				21.4 weeks (19–26)	21.0 weeks (12–38)		42.3 weeks (34–57)			
[8]	F	17–20	White			54							0.2
		40–45	White			54							0.26
[8]	F	17–20	Black			58							0.18
		40–45	Black			58							0.2
Thigh													
[2]	M	20–30	White	17–22		61–66	54 days (78)	98 days (136)		151 days (214)			0.33
[2]	F	20–30	White	10–17		69–74	22 days (40)	62 days (101)		84 days (141)			0.27

because the telogen hairs will not grow after treatment and will not become obvious until they switch into anagen.

Mild damage may be sufficient to cause an anagen follicle to shut down and prematurely convert into telogen. After resting, the follicle returns to anagen and continues its normal cycling. If no perifollicular scarring or other residual damage occurs, the follicle remains intact and produces the same quality of hair before and after treatment.

Significant follicular damage occurs when at least some of the critical structures in the hair growth apparatus are partially or completely destroyed. If this occurs, the hair attachment to the follicle loosens and it sheds shortly after treatment. Perifollicular scarring may develop and interfere with the recovery of the follicle. The hair may have a reduced size and pigmentation in the case that partial damage has been done [12].

The described gradation of the treatment effect is relative, because even radical hair removal methods such as the laser or electrolysis will not cause severe damage to all anagen follicles. When using lasers, for example, there may be little or no damage if the hair is white, the follicle is deep, or the skin is not sufficiently transparent to the laser emission. In addition, telogen hairs demonstrate less obvious clinical effect than do those in anagen [13,14].

MATERIALS AND METHODS

Statistical modeling methods capable of estimating the outcome of given events were used to develop a computer model that could predict hair growth kinetics. The computational algorithm was based additionally upon observations of hair growth data from the literature (Table 1) and a study center (ThermoLase Corporation, San Diego, CA). Several techniques were used at the study center to differentiate between hairs in various stages.

A distinguishing feature of anagen and telogen hairs is their difference in growth rate. If trimmed to 1–3 mm, anagen hairs will grow an additional 3–4 mm in 2 weeks, whereas the length of telogen hairs will not change. After differentiation, separate monitoring of anagen and telogen hairs is then possible.

Data collection at the study center was done on 10 subjects in 15 sites. This information was used as a basis for the development of the mathematical model and is not reported per se herein. The collection involved photography of test sites at each visit followed by trimming to 1–3 mm. At the 2- to 4-week follow-up examination, anagen and telogen hairs could be differentiated and counted, allowing a more precise evaluation of hair growth kinetics. In several studies, the anagen and telogen hairs were counted by using both high-resolution digital photographs (Kodak Professional DCS 420, Eastman Kodak Company, Rochester, NY) and a stereo dissecting microscope (Kodak SMZ-2T, Eastman Kodak Company). Although the microscopic technique provided greater accuracy with minimally pigmented and short hairs, the discrepancy between the photographic and microscopic counts rarely exceeded 10%.

Another evaluation procedure used included trimming, photographing, and counting the hairs followed by close shaving. Because the resting telogen hairs remained below the skin surface and were effectively invisible at the follow-up visit, only growing anagen hairs could be counted. This procedure, combined with the baseline hair counts, provided information similar to the previously described more accurate, but time consuming technique.

After data collection and literature evaluation (Table 1), mathematical equations relating the time of anagen and telogen to the anagen and telogen percentages were developed. This kinetic model could predict the results of undisturbed hair growth and was compared with experimental data from a simple shaving experiment (Fig. 1). The experiment included 10 subjects who were followed-up every 2 weeks for a total of 12 weeks. Test sites with easily identifiable hairs were chosen after differentiating those in anagen and telogen. Templates were then made for future site identification and baseline photography was done. Hairs were counted manually under the microscope and photographically at baseline and every 2 weeks for 12 weeks. The model compared with these experimental results was termed the "stationary model" because it predicted growth kinetics in hairs that continued undisturbed through their hair cycle.

Another situation was considered in which an intervention on the hairs had occurred. Prediction of hair growth after some disturbance to the hairs required the inclusion of additional variables in the statistical description, namely the degree of damage to the hair after the intervention. The addition of these variables made the model too complicated for simple mathematical formu-

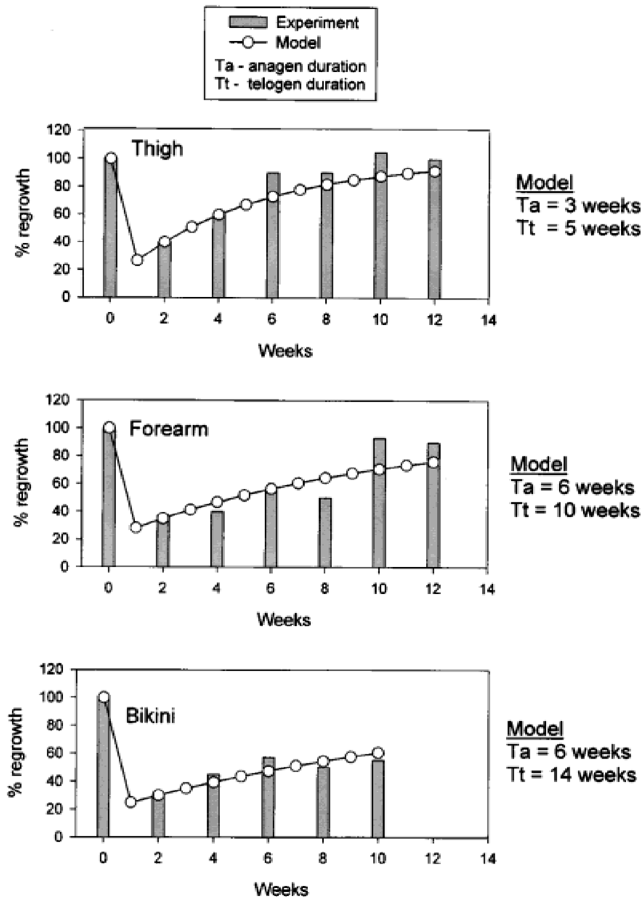


Fig. 1. Experimental hair regrowth data after shaving approximated by results from the stationary model.

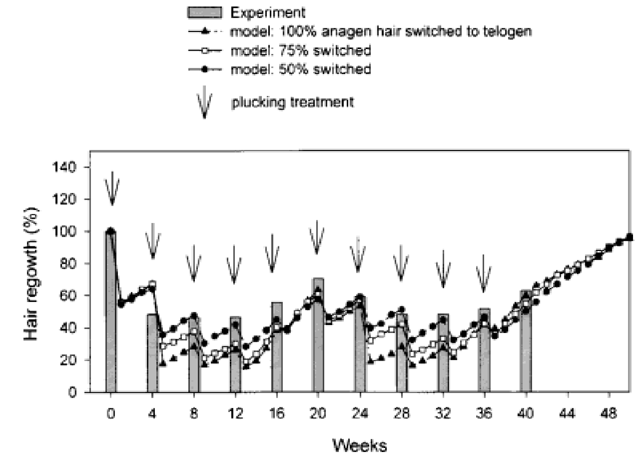


Fig. 2. Hair regrowth data from 10 axillary plucking treatments [18] compared with results from the nonstationary model. The closest approximation occurs when it is assumed that 50% of anagen hairs are switched to telogen with each treatment.

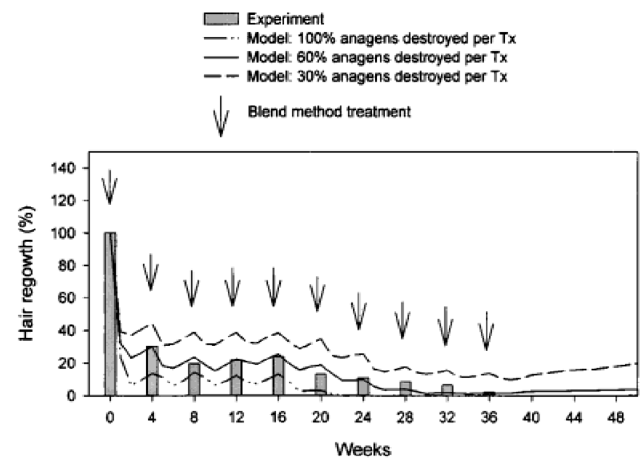


Fig. 3. Hair regrowth data from 10 axillary electrolysis/thermolysis treatments (the blend method) [18] compared with results from the nonstationary model. Assuming that 60% of anagen hairs are destroyed per treatment gives the best approximation of experimental results. Tx, treatment.

las, and a computerized model became necessary. The computerized model was developed and then tested against data from the literature (Figs. 2–4) and a study center (Fig. 5). The experiment at the study center was identical to the shaving experiment noted above except that five treatments at 4-week intervals were done with the Q-switched Nd:YAG laser (SoftLight, ThermoLase Corporation, San Diego, CA) in conjunction with a topical carbon suspension as previously described [15,16]. Twelve subjects with two test sites each were involved. Subjects were followed for 48 weeks. The model compared with these experimental results was termed the “nonstationary model,” because the hair cycles were disturbed and not allowed to continue through their normal progression.

HAIR GROWTH MODELS

Stationary Model

A stationary model is applicable if no treatment has been performed or the hair sustains no damage after treatment. In this model, a key assumption is that the initiation of individual hair cycles is a stationary Poisson process with a 1/e decay time Ta for anagen hairs and a Tt decay time for those in telogen. In particular, this means that individual hair cycles are not correlated or synchronized. Experimental data demonstrate that the “survival probability” of anagen hairs is governed by an exponential decay law [10]. Catagen hair kinetics can be also taken into account, although the model described in this section ignores catagen because of the relatively small number of catagen hairs. The total number

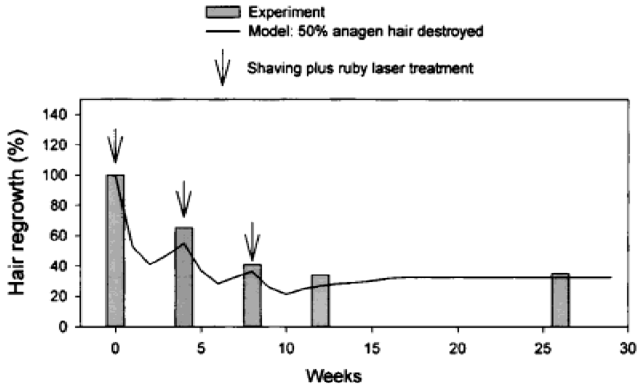


Fig. 4. Experimental hair regrowth data from sites receiving three ruby laser treatments at 4-week intervals [19] compared with results from the nonstationary model. The closest approximation to the actual results occurred when it was assumed that 50% of the anagen hairs were destroyed per treatment.

of hairs per unit area was assumed constant. Given percentages of anagen (Pa) and telogen (Pt) hairs, the conservation of the total number of hairs can be mathematically represented as follows:

$$\mathrm{Pa} + \mathrm{Pt} = 100. \tag{1}$$

A simple kinetic model describes the evolution of the anagen and telogen percentages with time (t):

$$\begin{aligned} d\mathrm{Pa}/dt &= -\mathrm{Pa}/\mathrm{Ta} + \mathrm{Pt}/\mathrm{Tt} \\ d\mathrm{Pt}/dt &= \mathrm{Pa}/\mathrm{Ta} - \mathrm{Pt}/\mathrm{Tt}. \end{aligned} \tag{2}$$

The steady state solution of this system of equations is:

$$\begin{aligned} \mathrm{Pa} + \mathrm{Pt} &= 100 \\ \mathrm{Pa}/\mathrm{Pt} &= \mathrm{Ta}/\mathrm{Tt}. \end{aligned} \tag{3}$$

The latter equation indicates that, because the duration of telogen is longer than the duration of anagen in most body areas, the percentage of telogen hairs is greater than that of those in anagen. For the scalp, the opposite is true. Most hairs on the scalp are in anagen because the duration of this phase is much longer than the duration of telogen. From the above solution, the steady state percentages of anagen (Pa^s) and telogen (Pt^s) hairs can be calculated explicitly in terms of the times Ta and Tt:

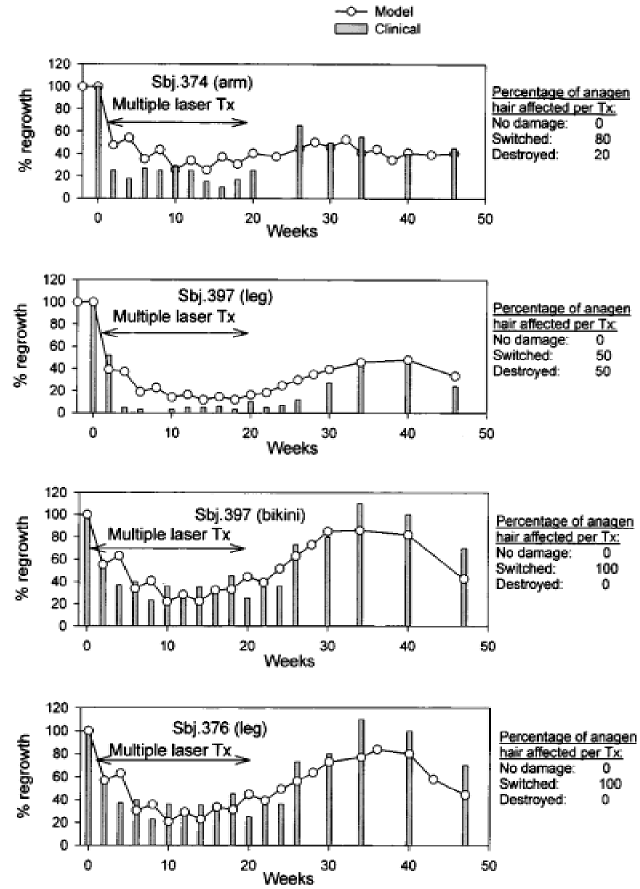


Fig. 5. Typical examples of experimental hair regrowth data from sites receiving five Q-switched Nd:YAG laser treatments at 4-week intervals compared with results from the nonstationary model. Varying the anagen switching and destruction percentages allowed close approximation of the actual results. Tx, treatment.

$$\begin{aligned} \mathrm{Pa}^s &= 100/(1 + \mathrm{Tt}/\mathrm{Ta}) \\ \mathrm{Pt}^s &= 100/(1 + \mathrm{Ta}/\mathrm{Tt}). \end{aligned} \tag{4}$$

In general, the model (equation 2) or its modification can be used whenever a noncorrelated cycling of hairs is undisturbed by treatment.

For instance, let us assume that the hair was closely shaved at time t = 0 and the hair regrowth was evaluated by counting visible hair at the skin surface. An instantaneous reduction of visible hairs will be Pt percent, because telogen hairs will not grow. The anagen hairs will keep growing at t > 0 and in due time, will switch into telogen. These new telogen hairs will be visible, so they will be counted. The hairs initially in telogen (old) at time t > 0 will start switching into anagen and grow, so that they also become visible. The

number of initial (old) telogen hairs (Pti) decay exponentially with time:

$$\text{Pti} = \text{Pt}^{s} * \exp(-t/\text{Tt}). \tag{5}$$

Modified kinetic equations for the percentages of countable hairs, including anagen (Pa) and new telogen (Pt) are:

$$\begin{aligned} d\text{Pa}/dt &= -\text{Pa}/\text{Ta} + (\text{Pti} + \text{Pt})/\text{Tt} \\ d\text{Pt}/dt &= \text{Pa}/\text{Tt} - \text{Pt}/\text{Tt}. \end{aligned} \tag{6}$$

Here Pa and Pt designate percentages of anagen and telogen hairs that have become visible at a time $t > 0$. The total percentage of hair regrowth (TPG) equals Pa+Pt and can be easily calculated:

$$\text{TPG} = 100 - 100/(1 + \text{Ta}/\text{Tt}) * \exp(-t/\text{Tt}). \tag{7}$$

Equation (6) shows that the total hair growth percentage initially equals that of anagen hairs at $t = 0$, but over time approaches 100%. Also, from equation (7) it can be seen that the duration of the telogen phase (Tt) determines how fast complete regrowth will occur. In body sites or individuals with a longer than normal telogen duration, a simple shaving can produce a substantial reduction in hair growth for an extended period of time.

Based on the model, the duration of telogen and anagen can be estimated experimentally in a time shorter than the entire hair cycle. Assuming that the total hair regrowth percentage (TPG2) was estimated at week 2 after shaving, equation (7) can be conveniently rewritten for practical use as follows:

$$\text{TPG}(t) = 100 - (100 - \text{TPG2}) * \exp(-(t - 2)/\text{Tt}) \tag{8}$$

where units for time t and Tt is weeks. The duration of telogen (Tt) can be estimated by fitting clinical hair regrowth data after shaving with equation (8). An estimate for the duration of anagen (Ta) then can be calculated from equation (3), provided the anagen to telogen ratio was found with the trimming technique described in the Materials and Methods section. Examples of hair regrowth data and their approximation by using the stationary model are shown in Figure 1.

Nonstationary Model

In the case of follicular treatment or cycle correlation, the stationary model discussed in the previous section is not valid and a different model must be developed. In this situation, a mathematical formulation of the model becomes more complicated and a computer model is appropriate. In this study, we shall refer to the nonstationary model as that which takes into account follicular treatment or the correlation of individual hair cycles. This finding is in contrast to the above stationary model that assumes no correlation or treatment.

In the nonstationary model, individual hair follicles are considered to be independent oscillators characterized by a certain duration of growth (anagen) and rest (telogen). If left alone, the follicles will continue through their cycles independently and will switch from anagen to telogen and back in a time corresponding to the individual duration of the two main phases of their cycle. Given a large group of the follicles, a certain distribution in the cycle duration will be observed. In the model described in this section, the distribution was assumed to be Gaussian with a 10–20% standard deviation from the average value. This assumption was based on data in the literature that suggest that this is a reasonable approximation of the actual distribution [3]. Another important characterization factor for this same group of hairs is their distribution with regard to the time individual follicles enter a new cycle. In the case that this time is completely random, the nonstationary and stationary models will produce identical results. The opposite case, in which the new cycles begin simultaneously, corresponds to a high degree of correlation between individual hair cycles. If the duration of anagen and telogen were the same for all follicles, there then would be a 100% correlation between the cycles over an infinite time period. Variations in the cycle duration between individual follicles and consecutive cycles of the same follicle will eventually cause complete loss of correlation between cycles of initially synchronized hairs.

A computer model has been developed that uses a statistical approach to simulate hair growth cycles. In the model, a large group of follicles initially cycling asynchronously was considered. The model simulated each follicle's evolution during a given time period. For example, the follicular evolution could be simulated over 52 weeks in 1-week increments. At week zero, each follicle was ascribed a status of either anagen or telogen such that the percentage of hairs in either phase corresponded to an expected value given by the pair of formulas (4). The time in anagen (Ta)

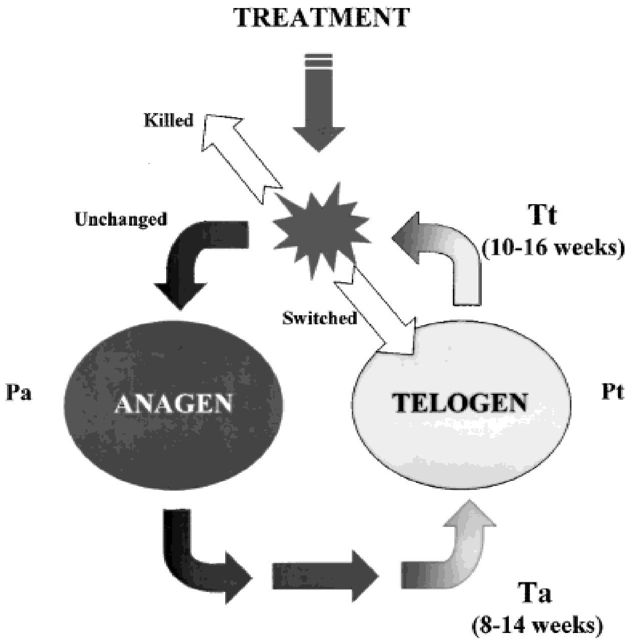


Fig. 6. A schematic representation of the nonstationary model of anagen hair growth kinetics after treatment.

and telogen (Tt) was varied at random between the follicles and between the consecutive cycles of each follicle. As a result, the Ta and Tt values had a Gaussian distribution with the means corresponding to experimental values found in the literature for specific body areas with a 10% standard deviation. As each follicle progressed through the model hair growth cycle, the follicular status could remain unchanged or be modified from anagen to telogen or inversely if the hair reached the end of the time corresponding to a particular growth phase. The follicular status was evaluated and modified based on the time spent in the current status when compared with individual values for Ta and Tt. Modifications were made at each 1-week increment of the model follicular evolutionary period. For instance, when the current status of a follicle is anagen and the time is greater than Ta, the follicle switches to telogen. Telogen follicles followed a similar pattern.

For anagen hair follicles, the hair growth cycle sequence could be disrupted at certain points in time if a laser or a nonlaser treatment was scheduled. The effect of such treatments was specified by ascribing the probability Wo that no damage was done to the follicle, the probability Ws of premature switching into telogen, and the probability Wd of permanent follicular damage (Fig. 6). The combination of these probabilities equals unity (Wo + Ws + Wd = 1) because no alternative outcomes were considered. By choosing different values for the probabilities, different treatment procedures could be simulated. For example, a combination of Wo = 1 and Ws = Wd = 0 was found to correspond to shaving. Another set, where Wo = 0.5, Ws = 0.5, and Wd = 0, appears to closely approximate the average results of waxing. The probability Wo = 0.5 may be interpreted as the probability of hair breakage during waxing and Ws = 0.5 as the chance of removing the entire hair by the "root."

Telogen follicles were assumed not to be affected by any treatment. This assumption was made because laser hair removal observations with the Q-switched Nd:YAG laser in humans and the long-pulsed ruby laser in animals support this contention [14,15]. Since the development of this model, it has been reported that human telogen follicles can be affected by long-pulsed ruby laser treatments [17], presumably only if they maintain an adequate concentration of the chromophore melanin. However, because this new information is not presently published and available for review, no further comment will be made. It should be noted that the assumption that telogen hairs are not affected would be expected to give a more conservative estimate of hair removal efficacy. Nonetheless, even with this assumption, the model still was able to closely approximate actual hair removal results.

A statistical decision making algorithm allowed simulation of the follicular modification as a result of treatment. The algorithm included the generation of a uniformly distributed random number (RN), ranging from 0 to 1 for individual anagen follicles. The decision whether the hair status should change was made by using the following criteria:

If RN < Wo, then the follicular status remains the same;

If Wo ≤ RN < (Wo + Ws), then the follicular status changes from anagen to telogen.

Otherwise, the hair was regarded as permanently damaged and was removed from the population during further simulation. At each step throughout the entire simulation process, the remaining number of follicles in anagen and telogen was calculated and the corresponding hair percentages were derived.

Laser and electrolysis are the only routinely used hair removal methods that can induce severe follicular damage. The performance of different devices and techniques can be quantitatively

characterized by approximating the results of individual and multiple treatments with the model and estimating the long-term hair loss per treatment. A virtual treatment procedure then can be developed and optimized by incorporating the measurement data into the nonstationary model.

Approximation of experimental hair removal data with the nonstationary model

The nonstationary model has been tested by approximating the hair growth data from clinical hair removal studies at a study center (ThermoLase Corporation) and in the literature. When necessary, a combination of several of the removal methods such as shaving and the laser was simulated to better approximate a particular treatment protocol.

Plucking

A detailed report on the results from repeated hair plucking sessions has been published by Urushibata and Kase [18]. Fourteen female Japanese subjects received 10 manual axillary plucking treatments at 1-month intervals. Experimental data presented in the study were simulated with the nonstationary model under the assumption that the average axillary anagen duration was 12 weeks and that of telogen was 16 weeks. A certain percentage of anagen hair was assumed to be only mildly damaged, yet sufficient enough to force growing hairs into a resting stage. The remaining hairs were assumed not to be affected. Modeling results are presented (Fig. 2) that consider anagen to telogen switching probabilities (Ws) to range from 1.0 (all anagen hair switched into telogen) to 0.5 (50% anagen hair switched to telogen and 50% remain unaffected). The modeling data fit the experimental data very well at Ws = 0.5. An interesting feature in both the experimental and simulation data is a regrowth peak at week 20. This finding may be attributed to the induction of a partial hair cycle correlation induced by plucking the hair. Switched telogen hairs tend to re-enter anagen at nearly the same time after a 14- to 18-week resting period.

Electrolysis/thermolysis

The above-cited study [18] also presented experimental data on the blend method of electrolysis for the same subject group and body area. Ten treatments at 1-month intervals were done before a substantial hair reduction was achieved. The nonstationary model was used to approximate this data (Fig. 3). The best fit case corresponds to probabilities of Wo = 40, Ws = 0, and Wd = 60. It is instructive to analyze the treatment results from the kinetic model standpoint. After significant initial improvement (week 4), no further improvement was observed until week 16, even though each treatment produced significant damage to the growing hairs. This 16-week period coincides with the duration of telogen. Although anagen hairs were efficiently destroyed by treatments, telogen hairs switching into anagen maintained hair regrowth from the time of the treatment initiation. After all hairs had cycled into anagen and were treated, an exponential decay in hair regrowth is observed.

Ruby Laser

Very little information has been published on the kinetics of hair regrowth after ruby laser treatment. In this study, to evaluate the model, we shall use data published by Williams et al. [19]. The clinical study protocol included three laser treatments 4 weeks apart and a 16-week follow-up after the last treatment. At each treatment, skin was shaved and lased with a ruby laser (Epilaser, Spectrum Medical Technologies, Inc., Lexington, MA) at 14–32J/cm^2. Treatment sites included the axillae, back, bikini line, and legs. Modeling of data from diverse body areas is a challenging task because of the differences in the kinetic parameters of hair growth. However, experimental and modeling data are shown in Figure 4. The kinetic parameters assumed for modeling were Ta = 12 weeks, Tt = 10 weeks, Wo = 0.5, Ws = 0, and Wd = 0.5. By using these parameters, the model provided a good approximation of the clinical results.

Q-Switched Nd:YAG Laser

The nonstationary mathematical model has been compared with experimental results derived from clinical trials with the Q-switched Nd:YAG laser (SoftLight, ThermoLase Corporation). The model has been applied to approximate the hair removal results with single and multiple treatments. Several examples are shown in Figure 5. The model proved to be capable of closely approximating clinical results by adjusting the three probabilities Wo, Ws, and Wd and the kinetic parameters Ta and Tt to correspond to a specific body area. Clinical data has shown that the Q-switched Nd:YAG laser consistently switches growing hairs into a resting stage. To approximate clinical data with the model in the leg and

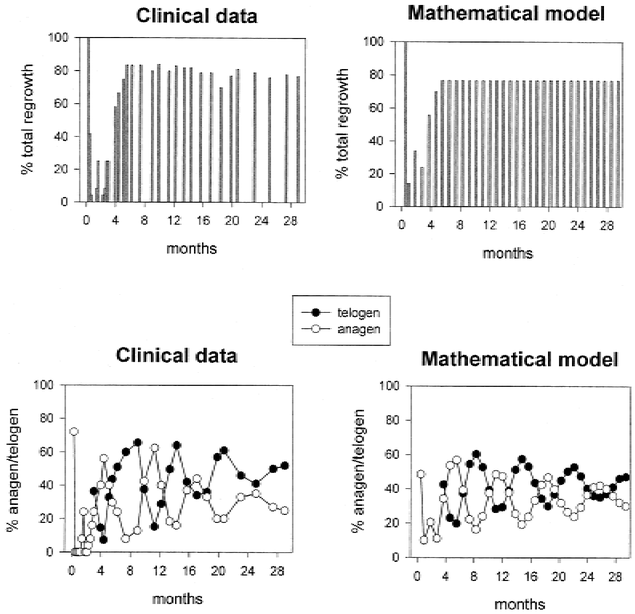


Fig. 7. An example of synchronization of the hair growth cycle in a subject after Q-switched Nd:YAG laser treatment, demonstrating the correlation between clinical and mathematical modeling data.

arm area, it was necessary to assume severe follicular damage had occurred. Assumptions of up to 30% anagen follicle destruction per treatment were necessary for accurate results in some cases. Occasionally, the probability needed to be as high as 50% (see Fig. 5, subject 397).

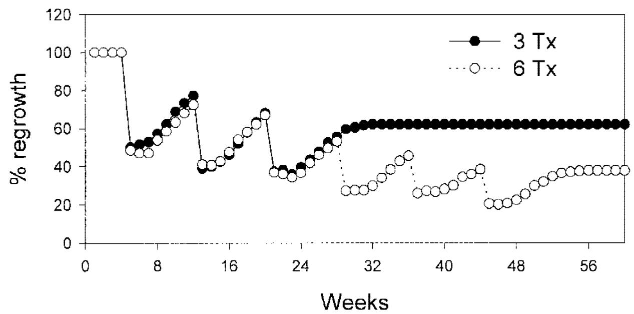
Another important effect of the Q-switched laser is a long-term oscillatory effect on hair growth kinetics after treatment. The effect becomes obvious only if the laser treated area is shaved periodically, e.g., monthly so that anagen hairs alone are counted. As the graphs in Figure 5 illustrate, a noticeable hair regrowth 3–4 months after treatments is followed by a significant hair growth reduction. This long-term effect represents a synchronization of individual hair growth cycles. Observations of the clinical study treatment results have demonstrated that single and multiple treatments induce alternating waves of growth and resting in the treatment area. The effect was initially predicted by the kinetic model and later confirmed clinically (Fig. 5).

An additional example of hair growth cycle synchronization can be seen in an individual followed-up for a 30-month period (Fig. 7). Clinical data are shown on the left, and the corresponding mathematical model data are shown on the right. The model assumed that 30% of anagen follicles were destroyed and 70% were switched to telogen with each treatment. The telogen hairs were assumed not to be affected.

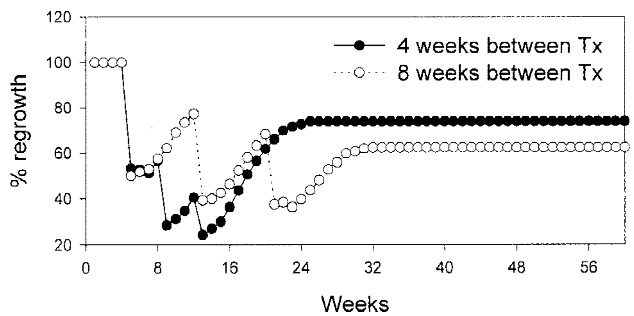
Two treatments with the Q-switched Nd:YAG laser were done at zero time and 2 months. After the treatments, hair numbers were counted at regular intervals as shown. Several interesting findings may be noted. In the top graphs of Figure 7, it can be observed that total hair numbers initially declined for a several month period. Subsequently, beginning about 6 months after the original treatment, the hair numbers remained fairly stable at a roughly 80% regrowth, corresponding to a 20% hair reduction. The actual and model percentage hair reduction is less than the assumed 30% destroyed anagen follicles because the total number of anagen follicles is less than the total hair number. There is a reasonably close correlation between the clinical and mathematical model data in this subject, but if one is not aware of the possibility of an oscillatory effect, it is not obvious when examining these data.

When counting anagen and telogen hairs individually, a cycling phenomenon can be seen clearly. Shortly after treatment, the number of anagen hairs declines to zero and gradually increases until another treatment is performed. After the second treatment, the number of anagen hairs eventually returns to a value slightly lower than the pretreatment value, but does not stay at this level. As can be seen, the anagen hair number begins to vary from about 20–60% with a periodicity of 3–4 months. This variance gradually decreases over time until the end of the observation period at 30 months. The number of telogen hairs also can be seen to vary after treatment but inversely with the number of anagen hairs. Again, the clinical and mathematical model data are in close agreement.

It is hypothesized that synchronization takes place because most anagen hairs enter telogen simultaneously after treatment. This is in contrast to the normal random pattern of follicular entry into anagen or telogen. The tapering of the variance in follicular anagen and telogen number is thought to occur because of variations in the hair growth cycle duration between follicles. This duration variation causes a gradual desynchronization to occur over time. The findings described in this section do not appear to be spurious because several other subjects followed for 12–18 months after Q-switched Nd:YAG laser treatment also have demonstrated a similar synchronization pattern.



a)



b)

Fig. 8. Examples demonstrating how the mathematical model can predict the results of different treatment protocols with the Q-switched Nd:YAG laser: (**a**) three or six treatments performed at 8-week intervals and (**b**) three laser treatments performed at 4- or 8-week intervals. Tx, treatment.

Modeling for the optimization of laser hair removal

The mathematical models described in this report have the potential to dramatically accelerate the research and development of laser hair removal procedures. The stationary model can be used to estimate the kinetic parameters of undisturbed hair growth. However, the nonstationary model must be used to optimize the treatment protocol for a particular hair removal device. An example of how the model can help to predict the treatment results and optimize the protocol with the Q-switched Nd:YAG laser is illustrated in Figure 8.

The optimal number of treatments is considered in Figure 8a. Three or six treatments are done at 8-week intervals then followed for 1 year. Under the assumption of a 30% kill rate (Wd = 0.3) for each individual treatment, it is evident that six treatments will give a greater and longer lasting hair reduction than will three. Other treatment variables, which will give different and perhaps better results, could also be considered and modeled.

Figure 8b shows the effect of lasing at the different time intervals of 4 and 8 weeks. Although results initially seem better when treating every 4 weeks, at the 1-year follow-up, the 8-week treatment interval demonstrates a superior effect. This finding is not a conclusion that necessarily would be reached intuitively, but is clearly suggested by the model and may be explained by an increased number of susceptible follicles at the longer treatment interval. Therefore, as these examples illustrate, changing and comparing specific variables with the model can help in the development of protocols that use the optimal number and interval of treatments.

CONCLUSION

A mathematical model such as that described in this study may prove useful in the research and development of laser hair removal devices. It seems possible to approximate with reasonable accuracy the results of a variety of hair removal methods as shown in this retrospective study. The model may also be useful for determining the best number and interval of treatments when using a particular procedure. The phenomenon of hair growth cycle synchronization observed both clinically and with the mathematical model may play a role in this determination. In addition, this model may be used as an adjunct in the development of new hair removal techniques. Finally, to further verify its validity, prospective studies that use this model should be undertaken.

REFERENCES

1. Olsen EA. Methods of hair removal. J Am Acad Dermatol 1999;40:143–155.
2. Seago SV, Ebling JG. The hair cycle on the human thigh and upper arm. Br J Dermatol 1985;113:9–16.
3. Saitoh M, Uzuka M, Sakamoto M. Human hair cycle. J Invest Dermatol 1970;54:65–81.
4. Edelstein-Keshet L. Mathematical models in biology. Boca Raton, Ann Arbor, London, Tokyo: CRC Press; 1988.
5. Sitharoma IS. Computer modeling of complex biological systems. Boca Raton, Ann Arbor, London, Tokyo: CRC Press; 1984.
6. Barman JM, Astore I, Pecoraro V. The normal trichogram of the adult. J Invest Dermatol 1965;44:233–236.
7. Blume-Peytavi U, Orfanos CE. Microscopy of the hair: the trichogram. In: Serup J, Jemec GBE, editors. Handbook of non-invasive methods and the skin. Boca Raton, Ann Arbor, London, Tokyo: CRC Press; 1995. p 549–554.
8. Altman PL, Dittmer DS. Tissue growth and renewal:

mammals. In: Altman PL, Dittmer DS, editors. Biology data book, 2nd ed, vol I. Bethesda, MD: Federation of the American Society of Experimental Biology; 1972. p 107.
9. Trotter M. The life cycles of hair in selected regions of the body. Am J Phys Anthropol 1924;7:427–437.
10. Courtois M, Loussouarn G, Hourseau C, Grollier JF. Periodicity in the growth and shedding of hair. Br J Dermatol 1996;134:47–54.
11. Courtois M, Loussouarn G, Hourseau C, Grollier JF. Aging and hair cycles. Br J Dermatol 1995;132:86–93.
12. Dierickx CC, Grossman MC, Farinelli WA, Anderson RR. Permanent hair removal by normal-mode ruby laser. Arch Dermatol 1998;134:837–842.
13. Kolinko VG, Littler CM. The influence of the anagen:telogen ratio on laser hair removal efficacy. Lasers Surg Med 1999;11(Suppl):60.
14. Lin T-YD, Manuskiatti W, Dierickx CC, Farinelli WA, Fisher ME, Flotte T, Baden HP, Anderson RR. Hair growth cycle affects hair follicle destruction by ruby laser pulses. J Invest Dermatol 1998;111:107–113.
15. Goldberg DJ, Littler CM, Wheeland RG. Topical suspension-assisted Q-switched Nd:YAG laser hair removal. Dermatol Surg 1997;23:741–745.
16. Nanni CA, Alster TS. Optimizing treatment parameters for hair removal using a topical carbon-based solution and 1064-nm Q-switched neodymium:YAG laser energy. Arch Dermatol 1997;133:1546–1549.
17. Dierickx CC, Campos VB, Lin D, Farinelli W, Anderson RR. Influence of hair growth cycle on efficacy of laser hair removal. Lasers Surg Med 1999;11(Suppl):21.
18. Urushibata O, Kase K. A comparative study of axillary hair removal in women: plucking versus the blend method. J Dermatol 1995;22:738–742.
19. Willams R, Havoonjian H, Isagholian K, Menaker G, Moy R. A clinical study of hair removal using the long-pulsed ruby laser. Dermatol Surg 1998;24:837–842.